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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,248	02/27/2007	Suk-Wah Tam-Chang	028.0002-US00	3055

92049 7590 11/30/2011

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
11/30/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/578,248	TAM-CHANG ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-15 and 25-43* is/are pending in the application.

5a) Of the above claim(s) *1-15 and 25-40* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *41-43* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *12 January 2011* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-15 and 25-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 29 June 2009.

Drawings

2. The drawings were received on 12 January 2011. These drawings are acceptable.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 41 and 43 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the abstract, and pages 2-5 of the disclosure, and, by extension, application of 35 USC 112, fourth paragraph, to claims 41 and 43 when taken in light of claim 42.

5. As presently worded, the invention of claim 42 is recognized as fairly encompassing the disclosed invention. Given that a dependent claim must further limit the claim from which it depends, claim 41, and by extension, claim 43 which depends from claim 41, must encompass an embodiment where hybridization of a target nucleic acid sequence to the nucleic acid sequence

complementary to the target nucleic acid sequence does not disrupt formation of the stem-loop. Such an embodiment, upon review of the disclosure, is not considered to be what applicant regarded as being their invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/36668 A1 (Sauer et al.) in view of US Patent 6,379,892 B1 (Kacena) and Crockett & Wittwer.

10. Claim 41 is the only independent claim pending and under consideration. For convenience, claim 41 is reproduced below.

> 41. (New) A nucleic acid complex for detecting a target nucleic acid sequence comprising two discrete sequences:
>
> 1) a fluorophore-labeled reporter comprising a fluorophore attached to an oligonucleotide sequence;
>
> 2) an oligonucleotide having a stem-loop structure having a first stem section, a second stem section, and a tail sequence from the second stem section, wherein;
>
> a) the first stem section comprises at least one guanosine base,
>
> b) the tail sequence is complementary to the fluorophore-labeled reporter oligonucleotide sequence,
>
> c) the loop comprises a sequence complementary to the target nucleic acid sequence; and
>
> wherein the fluorophore-labeled reporter is hybridized to the tail sequence of the oligonucleotide having a stem-loop structure, and the at least one guanosine base in the first stem section quenches the fluorophore.

11. Attention is directed to MPEP 904.01.

> The breadth of the claims in the application should always be carefully noted; that is, the examiner should be fully aware of what the claims do not call for, as well as what they do require. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). See MPEP § 2111 - § 2116.01 for case law pertinent to claim analysis.

12. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

13. For purpose of examination, the "first stem section" and the "second stem section" have been construed as being immediately adjacent to one another such that they go to form but a single stem, which is part of the recited "stem-loop structure."

14. Sauer et al., in the abstract, teach:

> The invention relates to an oligonucleotide (10) which serves as nucleic acid probe and consists of a loop section (18) that is provided with a loop sequence being complementary to a target sequence of the nucleic acid molecule. Said oligonucleotide also consists of stem sections (14, 16) that are arranged on both ends of the loop section and can hybridise with each other for closing the oligonucleotide (10) in such a way that said oligonucleotide forms a loop. Only one of the stem sections (14) is labelled with a fluorescence colour (12). The remaining stem section (16) contains guanosine (6). Guanosine quenches the fluorescence of the colour (12) by means of a photo-induced transfer of electrons provided that colour (12) and guanosine (6) are present in sufficient spatial proximity. This is the case when stem sections (14, 16) hybridise with each other and close the oligonucleotide (10) to form a loop. When the loop section (18) hybddises [*sic*] with the target sequence section of the nucleic acid molecule, however, the oligonucleotide (10) that is folded to form a loop opens and the distance between colour (12) and guanosine (6) increases. Quenching of fluorescence is thus prevented. The oligonucleotide can be detected by the fluorescence thereof. The strength of fluorescence is s specific measure for the presence of nucleic acid molecules having the target sequence.

15. While Sauer brings the fluorophore-labeled oligonucleotide into sufficient proximity of the guanosine residue so to achieve quenching, the fluorophore and guanosine residues are all on

the same oligonucleotide. Additionally, while Sauer do have a tail region, it is comprised of any number of guanosine residues (note the "$(G)_n$" in the illustration).

16. Kacena teaches in column 10 that her probe may comprise a stem region, a loop region as well as a tail region, and that the "target binding sequence" may be found in the loop region. As disclosed therein, when the target nucleic acid hybridizes to the target binding sequence, the stem-loop secondary structure is disrupted.

17. Kacena, column 12, teach that the unfolding of the secondary structure as a result of hybridization to the target nucleic acid, is detected by a change in fluorescent label.

18. Crockett and Wittwer teach at length of hybridizing two discrete nucleotide sequences (oligonucleotides) together and that by so doing, one is able to achieve quenching of a fluorescent label by bringing the fluorescent label into proximity of guanosine residues, which are present in the second (complementary) oligonucleotide.

19. Crockett and Wittwer, abstract, teach a method of performing hybridization between complementary oligonucleotides where the fluorescent label, bound to one oligonucleotide, is quenched by a guanosine residue in the complementary (hybridized) oligonucleotide. Crockett and Wittwer also teach that by using one guanosine residue one can achieve "a 25% in fluorescence," and that "[a]dditional Gs can increase quenching to about 40%."

20. It would have been obvious to one of ordinary skill in the art at the time of the invention to have modified the oligonucleotide probe of Sauer by modifying the tail region such that the fluorophore-labeled oligonucleotide sequence that hybridizes to the quenching oligonucleotide sequence, and thereby forms a stem section, is actually a separate/discrete oligonucleotide (Crockett and Wittwer combined with Kacena). Said ordinary artisan would have been so

motivated by presenting the fluorophore label on a separate oligonucleotide, the label can be prepared separately and be used in any number of different assays as a common or shared reagent, thereby simplifying the manufacturing and assay process.

21. Said ordinary artisan would have had a most reasonable expectation of success as all reagents are being used in a manner consistent with their known properties, e.g., complementary nucleotide sequences hybridize to one another; target sequences, when bound to the loop region, can disrupt the stem section; and guanosine residues quench fluorescent signal, and that by adding additional guanosine residues, the degree of quenching observed is enhanced.

22. In view of the well-developed state of the art, and the guidance provided, said ordinary artisan would have been both amply motivated and would have had a most reasonable expectation of success. Accordingly, and in the absence of convincing evidence to the contrary, claims WO 01/36668 A1 (Sauer et al.) in view of US Patent 6,379,892 B1 (Kacena) and Crockett & Wittwer.

Conclusion

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634